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A SIMPLE SPECTROPHOTOMETRIC METHOD FOR THE DETERMINATION OF CAPTOPRIL IN PHARMACEUTICAL PREPARATIONS USING AMMONIUM MOLYBDATE
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resis [29], conductometry [30], coulometry [31], voltammetry [32] and potentiometry [33].

However, batch methods are generally time-consuming and laborious. In addition, chromatographic methods are slow and require expensive and complicated instrumentation, features that make them unattractive to routine analysis. Titrimetric method has suffered from a lack of specificity and sensitivity, under certain circumstances, such as the presence of unsaturated organic compounds.

Obviously, because of its low operating costs, simple equipment, as well as the widespread use of common laboratory, spectrophotometry has been an important analytical method to the chemical workers of analysis. It is very significant to find a rapid, accurate and simple method to determine captopril in the researches of the clinical medicine. Thus, spectrophotometric methods have also been described for the determination of CPT in the pure form and in pharmaceutical formulations [27, 34 – 42]. A UV spectrophotometric procedure has been used for the determination of CPT in bulk drug and tablets in the presence of iodine, where the indirect quantization of the product was carried at 351 nm [34] This method present low selectivity, as all unsaturated compounds display one or more bands in that region of the spectrum. The CPT has been determined in the area of the visible after the reaction with iodine [34], ferric chloride in presence of 2,2'–bipirydil [34] and potassium ferricyanide [35], Pd(II) [27, 36, 37], Co(II) in presence of 2,2'-dipyridil-2-pyridylhydrazone [38], N–(1–naphtyl) ethylenediamine in acid media (nitrous acid) [39], Folin-Ciocalteu reagent [40, 41] and molybdophosphoric acid [42]. This last procedure can only be used for the determination of CPT in pure forms, because the presence of the most common excipients in pharmaceutical formulations (glucose, fructose, lactose, sucrose, starch) they interfere seriously in this method. Such interferences, no studied by the authors, they were confirmed starting from preliminary tests accomplished at our research laboratory. However, no spectrophotometric method for determination of CPT based on the reduction reaction of ammonium molybdate has been reported.

Salts of molybdenum (VI) have been used as oxidizing agents in the spectrophotometric determinations of a number of substances of pharmaceutical interest. Tetracyclines have been assayed by using sodium molybdate [43, 44]. Molybdophosphoric acid has been applied in the determination of cephalosporins [45, 46], levodopa, carbidopa, α-methyldopa, isoniazid and acetaminophen [47]. The same reagent has also been applied successfully for the determination of phenothiazines [48, 49].

In this work, we report a novel, simple, rapid, cost-effective, precise, sensitive and accurate spectrophotometric method that is ideal for routine analysis of CPT in pharmaceuticals. Additionally, the proposed technique was ascribed to the fact that they are easily and widely used in laboratory analysis in addition to being economical in terms of their implementation and maintenance.

The proposed method is based on reaction of reduction of ammonium molybdate for the group thiol of CPT in acid media. The measurement of absorbance is made spectrophotometrically at 407 nm. The results agreed fairly well with those obtained by the USP standard procedure [23] at 95% confidence level. In this method, the CPT has been determined by volumetric titration, where the oxidation of the thiol group through iodometric titration.

Experimental

Apparatus

A HP 8453 spectrophotometer with 1 cm matched silica cells was used for all absorbance measurements. Volume measurements were made with plunger-operated pipetters (25–250 μL and 100–1000 μL) and Metrohm model 665 automatic burettes. All experiments were performed in a thermostated room (25±1) °C.

Reagents and solutions

For the preparation of the solutions and samples, deionised water (conductivity > 1μS cm^{-}

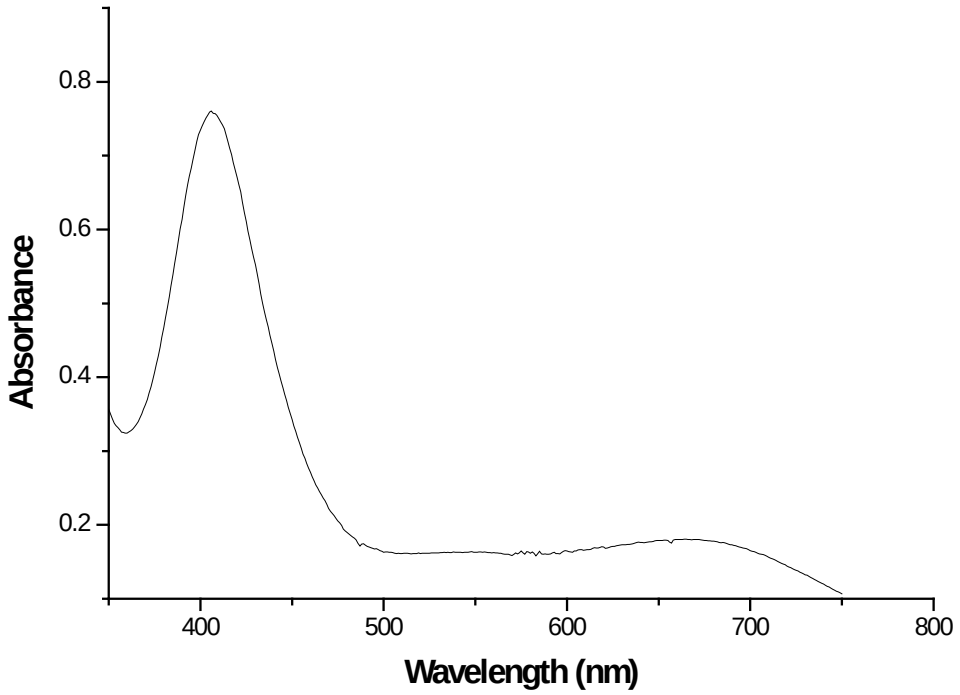

Figure 2. Absorption spectrum of the reaction product. Captopril final concentration = 1.61 x 10^{-3} mol l^{-1}; optical path = 1 cm. Measurements taken at 25 °C against the reagent blank after stoppered to room temperature for 30 min, as described in the recommended procedure.

Optimization of different experimental parameters and stability

The optimum conditions were established based on the development of maximum colour intensity and stability on variation of parameters affecting captopril oxidation and the coupled colour reaction with ammonium molybdate.

Using different concentrations of H_2SO_4, it was found that maximum colour intensity and stability were obtained by developing the reactions in 8.73 mol l^{-1} H_2SO_4, as described in the recommended procedure. At higher concentrations of H_2SO_4, the absorbance was found to decrease, whereas, below of this concentration the colour became unstable and the colour intensity diminished. Other acids were also studied for production of colour and it was found that no colour reaction was produced with acids like acetic acid, phosphoric acid and nitric acid, whereas, with hydrochloric acid a very light yellow colour was obtained which was unstable.

Ammonium molybdate was used as a colour producing reagent. The adopted ammonium molybdate concentration (2%) was found to be sufficient for providing maximum and repeatable colour intensity, when the concentration of this reagent was above or below of this concentration the absorbance was found to decrease.

The order of addition of the reactants recommended in the general procedure produced quantitative results. Any other order was found to produce deviant results and the colour intensity diminished.

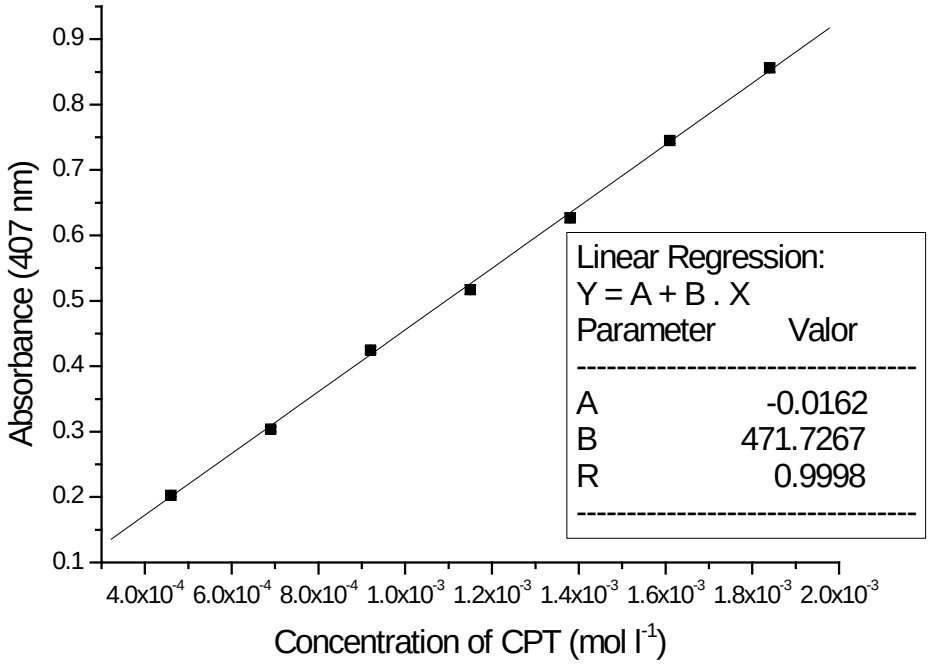

Figure 4. Analytical curve for determination of captopril.

Effected of interferents

To assess the use fullness of the proposed method, the effect of the common components (additives, adjuvants and excipients) witch often accompany captopril in tablet dosage formulations (lactose, microcrystalline cellulose, croscarmellose sodium, starch and magnesium stearate) were investigated using the developed method. The ratios of the concentrations of CPT to those excipient substances were fixed at 1.0 and 10.0. No interferences were observed in the presence of the substances tested.

Analytical applications, recovery and repeatability studies

In order to assess the utility of the presently developed method it was applied to the estimation of captopril in several pharmaceutical forms. The samples were prepared using the developed method. Then, the proposed method was successfully applied for CPT determination in six tablet formulations. The results, presented in Table 1, compare favorably with the official method of the United States Pharmacopoeia [23] at 95% confidence level. The results were subjected to a paired comparison test [52], the data of *t* and *F* ratios show no significant differences between the results of the proposed and the official methods, indicating very good accuracy and precision.

Table 2. Recovery data for captopril spiked to pharmaceuticals

Sample	Added (mg l^{-1})	Found (mg l^{-1})	Recovery (%) [a]
A	100.0 125.0 150.0	99.9 127.3 151.8	99.9 101.8 101.2 μ [a] = 100.9 ± 1.0
B	100.0 125.0 150.0	101.1 126.0 151.4	101.1 100.8 100.9 μ [a] = 100.9 ± 0.2
C	100.0 125.0 150.0	100.1 125.2 150.4	100.1 100.2 100.3 μ [a] = 100.2 ± 0.1
D	100.0 125.0 150.0	100.9 125.9 149.3	100.9 100.7 99.5 μ [a] = 100.4± 0.8
E	100.0 125.0 150.0	100.2 126.3 148.9	100.2 101.0 99.3 μ [a] = 100.2 ± 0.8
F	100.0 125.0 150.0	100.0 125.1 151.0	100.0 100.1 100.7 μ [a] = 100.3 ± 0.4

[a] Average ± standard deviation (SD) of three determinations.

To examine the repeatability of the procedure, replicate (n = 10) determinations were made on the same solution containing equivalent to 1.38 x 10^{-3} mol l^{-1} of CPT (300 mg l^{-1}). The relative standard deviation (RSD) at this concentration level was 1.2. This is good evidence of repeatability of the proposed method.

Conclusion

The proposed method results a simple, sensitive, inexpensive, precise and accurate analytical technique to determine captopril in commercial pharmaceutical preparations with satisfactory recoveries. Statistical comparison for the results of the proposed method with the official reported method indicates that there is no significant difference, at 95% confidence level, with regard to accuracy and precision. Additionally, it fulfills all the main demands of routine analysis as it is robust, has low instrumentation and operational cost in comparison to chromatographic methods and it doesn't request pretreatment of the sample.

When applied to the assay of various tablet dosage forms, its advantage is in that it does not

[23] United States Pharmacopeial Convention, The United States Pharmacopeia: The national formulary: captopril, 24th edn., Revision. Rockville, 2000, p. 296.
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